fluorescence images by using the analysis software Harmony (manufactured by PerkinElmer), and YAP protein-AlexaFluor®647 fluorescence intensity and TAZ protein-AlexaFluor®555 fluorescence intensity in each region were extracted. Furthermore, the ratio of the fluorescence intensity of the cell nucleus region to the fluorescence intensity of the cytoplasmic region was calculated from the extracted values. This time, the case where the fluorescence intensity ratio was 1.4 or more was defined as the cell population in which the YAP protein and the TAZ protein were transferred into the nucleus, and the ratio thereof was calculated.

[0367] The relative value of the calculated ratio of the cell population with respect to the control group (DMSO) was calculated, and it was found that the cell population increased 6 times or more for YAP protein and 1.5 times or more for TAZ protein by the addition of the following compound. Therefrom it was clarified that the specific compound used in the present invention has an action of promoting the nuclear translocation of the YAP protein and TAZ protein.

Compounds with 6 times or more increase in cell population with nuclear translocation of YAP protein:

k-1:B-1, GA-002A, k-1:J-1, k-1:H-1

[0368] Compounds with 1.5 times or more increase in cell population with nuclear translocation of TAZ protein:

k-1:B-1, GA-002A, k-1:J-1, k-1:H-1

[Example 13] YAP Phosphorylation Inhibitory Action of the Compound of the Present Invention

[0369] Human ovarian cancer cell line SKOV3 (manufactured by DS Pharma Biomedical Co., Ltd) was precultured (single layer culture) in a 15% FBS-containing McCoy's 5a medium (manufactured by Sigma Ltd. Aldrich). The above-mentioned cells in the logarithmic growth phase were washed with PBS, a 0.25% (w/v) trypsin-1 mmol/L ethylenediaminetetraacetic acid (EDTA) solution (manufactured by Fujifilm Wako Pure Chemical Corporation) was added, and adherent cells were detached by incubating at 37° C. for 3 min. The above-mentioned medium was added and the mixture was centrifuged and resuspended in the same medium.

[0370] According to the method of patent document (WO 2014/017513), a composition of 10% FBS-containing DMEM medium (Phenol-red free, manufactured by FUJIFILM Wako Pure Chemical Corporation) containing 0.015% (w/v) deacylated gellan gum (KELCOGEL CG-LA, manufactured by SANSHO Co., Ltd.) was prepared using FCeM-series Preparation Kit (manufactured by FUJIFILM Wako Pure Chemical Corporation). Then, various cells prepared above were suspended in the above-mentioned medium composition (3D conditions) added with deacylated gellan gum or a medium without the addition (2D conditions), and seeded on a 50 μL/well (manufactured by Corning Incorporated, 96 well flat bottom plate, #3585, 2D conditions) or 25 μL/well (manufactured by Corning Incorporated, 96 well low adhesion flat bottom plate, #3474) at 100000 cells/well. The plate was allowed to stand at 37° C. in a 5% CO_2 incubator, and the compound of the present invention diluted with the medium at 2 or 6 times the final concentration, DMSO, or the medium alone was added to the plate 3 hr after the seeding at 50 μL/well (2D conditions) or 5 μL/well (3D conditions) to make the final concentration of each compound 10 μM. After culture at 37° C. in a 5% CO_2 incubator for 1 hr, the supernatant was aspirated, supplemented Lysis buffer (1-fold concentration, manufactured by Cisbio, YAP-total kit or YAP phospho-S127 kit) (50 μL) was added under 2D conditions, and supplemented Lysys buffer (4-fold concentration) (10 μL) was added to the culture supernatant under 3D conditions, and the mixture was stirred by a plate shaker for 30 min. Thereafter, the plate was centrifuged, 16 μL of the supernatant was transferred to a 384-well white plate (Corning, #4512), and each antibody solution (pYAP d2 antibody or Total-YAP d2 antibody, and pYAP Cryptate antibody or Total-YAP Cryptate antibody) included in the kit was added at 4 μL/well in total, and the mixture was allowed to stand at room temperature overnight. As a blank control, pYAP Cryptate antibody or Total-YAP Cryptate antibody alone was added to cells free of stimulation with compound and the mixture was treated in the same manner (Non-treatment). The next day, the wavelengths at 665 nm and 615 nm were measured in the HTRF mode of EnVision (manufactured by PerkinElmer).

[0371] The obtained signal was calculated as follows. Ratio=signal (665 nm)/signal (615 nm)×10000, ΔR=Signal (Ratio)−Background fluorescence, and the relative value with respect to ΔR of the compound non-addition group (Non-treatment) as 100% was calculated, and the phosphorylated YAP amount or total YAP amount by each compound was evaluated.

TABLE 13

	phosphorylated YAP (%)	total YAP (%)
2D condition		
Non-treatment	100	100
DMSO	99	100
k-1:B-1	14	89
k-1:H-1	38	94
k-1:J-1	13	86
GA-002A	10	86
GA-005A	10	91
3D condition		
Non-treatment	100	100
DMSO	106	97
k-1:B-1	31	99
k-1:H-1	80	107
k-1:J-1	30	109
GA-002A	14	105
GA-005A	10	107

[0372] As shown in Table 13, it was shown that k-1:B-1, k-1:H-1, k-1:J-1, GA-002A, and GA-005A have a YAP phosphorylation inhibitory action under both 2D and 3D culture conditions.

[Example 14] Inflammation Suppressive Effect on Colitis Model Mouse

[0373] Colitis model administered with dextran sulfate sodium (DSS) (manufactured by FUJIFILM Wako Pure Chemical Corporation) was produced as described below. The length of the large intestine is used as a morphological parameter in the evaluation of colitis, and the large intestine shortens according to the degree of inflammation. Therefore, the anti-inflammatory effect of the compound was evaluated by comparing the length of the large intestine.